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EXAMINER	
SPIEGLER, ALEXANDER H	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 12/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/554,772	PETIT ET AL.	
	Examiner	Art Unit	
	Alexander H. Spiegler	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 September 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

1. This action is in response to Applicants' response, filed on September 30, 2004. Currently, claims 11-17 are pending and are rejected herein. This action contains new rejections that were necessitated by Applicants' amendments. Accordingly, this action made FINAL. Any objections and rejections not reiterated below are hereby withdrawn. It is noted that all previous rejections have been withdrawn, as the previous rejections were directed to Claims 3-6 and 8-10, which have been canceled.

THE FOLLOWING ARE NEW GROUNDS OF REJECTION NECESSITATED BY APPLICANTS AMENDMENTS TO THE CLAIMS

Claim Rejections - 35 USC § 112

Indefiniteness

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 11-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 11-17 are indefinite because claim 11 is drawn to a method for *preventing* platelet aggregation in a patient; however, the final step is for administering an effective amount of a ketolide sufficient to *inhibit* platelet aggregation in said patient. The claims do not set forth the relationship between preventing platelet aggregation in a patient and inhibiting platelet

aggregation in said patient. Therefore, it is not clear as to whether the claims are intended to be limited to a method of preventing platelet aggregation in a patient or for administering an effective amount of a ketolide sufficient to inhibit platelet aggregation in said patient.

New Matter

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 11-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Applicants have amended the claims to recite, "a method for preventing platelet aggregation in a patient." However, this recitation does not appear in the specification, nor is there support for this recitation in the specification. Accordingly, the newly added claims constitute new matter. If Applicants traverse this rejection, it is respectfully requested that Applicants provide support for this recitation (by specific page and line number).

Scope of Enablement

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 11-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for 1) a method of treating a human with atherosclerosis, in which *Chlamydia pneumoniae* infection appears to play a role in the development of the atherosclerosis, using the ketolides of the claimed invention, and 2) a method of inhibiting in vitro platelet aggregation, does not reasonably provide enablement for preventing platelet aggregation in a patient comprising administering to a patient in need thereof an effective amount of a ketolide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

MPEP 2164.01 states:

> Even though the statute does not use the term 'undue experimentation,' it has been interpreted to require that the claimed invention be enabled so that any person skilled in the art can make and use the invention without undue experimentation.

In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

The *Wands* court outlined several factors to be considered in determining whether a disclosure would require undue experimentation. These factors include, but are not limited to:

> (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Id. at 1404.

In the instant case, the specification does not enable one of skill in the art to make and use the claimed invention for the following reasons:

(1) ***Nature of the Invention & Breadth of the Claims***

The claims are drawn to a method of "preventing" platelet aggregation in a patient comprising administering to "a patient in need thereof" an effective amount of a ketolide or its non-toxic, pharmaceutically acceptable salts sufficient to inhibit platelet aggregation in said patient.

Accordingly, the claims are drawn to "preventing" platelet aggregation in a patient (e.g., human) comprising "administering to a patient" (i.e., an in vivo administration) in need thereof an effective amount of a ketolide or its non-toxic, pharmaceutically acceptable salts sufficient to inhibit platelet aggregation in said patient. Furthermore, the claims are also drawn to methods of "preventing" platelet aggregation in a patient (e.g., human having a platelet aggregating condition, e.g., atherosclerosis) who does not have a *Chlamydia pneumoniae* infection.

(2) ***Relative Skill of those in the Art, State of the Prior Art, Amount of Direction or Guidance Presented & Presence or Absence of Working Examples***

The specification teaches that the ketolides of the invention are only active (in vivo) against *Chlamydia pneumoniae*, and that *Chlamydia pneumoniae* "appears" to play a role in atherosclerosis. See page 6, lines 28-35. Specifically, the specification states,

> The infectious agent *Chlamydia pneumoniae* appears to play a role in the development of atherosclerosis in man. The ketolides are active against *Chlamydia pneumoniae*. As a result, the anti-infectious properties against *Chlamydia pneumoniae* which are associated with their anti-platelet aggregating activity allow them to be used to combat the development of atherosclerosis."

(See page 6, lines 28-35). Accordingly, the specification teaches the ketolides are active against *Chlamydia pneumoniae* infection *in man*.

Therefore, the specification teaches the following syllogism:

Chlamydia pneumoniae appears to play a role in the development of atherosclerosis (e.g., a platelet aggregating condition) in man. Ketolides are active against *Chlamydia pneumoniae.* Therefore, ketolides can be used to treat atherosclerosis (e.g., a platelet aggregating condition).

Accordingly, the specification's assertion of treating atherosclerosis is based solely on the anti-*Chlamydia pneumoniae* activity of the ketolides. Thus, the specification provides guidance as to the treatment of humans having atherosclerosis in which a *Chlamydia pneumoniae* infection appears to play a role in the development of the atherosclerosis. However, the specification does provide any guidance as to treating any individual having atherosclerosis and who does not have a *Chlamydia pneumoniae* infection.

In addition, the specification teaches a single example demonstrating an *in vitro* platelet aggregation test. See pages 7-9. This Example demonstrates the comparison of the effect of "Product P" and aspirin in an in vitro platelet aggregation test, wherein the test is performed on blood taken from rabbits. Specifically, the table on page 9 shows that at differing concentrations, Product P and aspirin have different levels of platelet aggregation inhibition. For example at a concentration of 10^{-7} M, Product P has a 7% platelet aggregation inhibition, at a concentration of 10^{-6} M, Product P has a 42% platelet aggregation inhibition, at a concentration of 10^{-5} M Product P has a 73% platelet aggregation inhibition, etc. See the table on page 9. The specification also states, "P_1, P_2 and P_3 ...also show 'good activity' on this in vitro platelet aggregation test." See page 9, lines 21-23.

However, the example does not demonstrate the "prevention" of antiplatelet aggregation *in a patient* (e.g., human). Furthermore, the specification does not provide any correlation between this assay and "preventing" antiplatelet aggregation or "preventing" an antiplatelet

aggregating condition (e.g., atherosclerosis). In addition, it is not clear what is meant by or what constitutes "good activity."

In order to determine whether the administration of the compounds of the present invention prevent platelet aggregation in a patient (e.g., human), a skilled artisan would necessarily have to monitor the individuals for a long period of time (i.e., many years) to determine whether they developed or did not develop platelet aggregation. The specification does not teach such monitoring. In fact, the recitation of "preventing" denotes that once the ketolides are administered to a patient, said patient will never suffer from platelet aggregation. The specification does not teach any in vivo trials suggesting that a patient who received treatment of the claimed ketolides would ever suffer from platelet aggregation.

Therefore, while the specification teaches the treatment of humans having atherosclerosis in which a *Chlamydia pneumoniae* infection appears to play a role in the development of the atherosclerosis and that P- P_3 shows "good activity" in an in vitro platelet aggregation test, the specification does not provide the skilled artisan the requisite guidance for "preventing" platelet aggregation in a patient (e.g., human) comprising "administering to a patient" (i.e., an in vivo administration) in need thereof an effective amount of a ketolide or its non-toxic, pharmaceutically acceptable salts sufficient to inhibit platelet aggregation in said patient. Furthermore, the specification does not provide the skilled artisan the requisite guidance for "preventing" platelet aggregation in a patient (e.g., human having a platelet aggregating condition, e.g., atherosclerosis) who does not have a *Chlamydia pneumoniae* infection.

It is noted that the art teaches the use of antiplatelet aggregation tests are unpredictable and take long periods of time to fully develop adequate results. Specifically, Kullo et al. (MAYO Clinic Proceedings (2000) 75(4): 369-80, previously cited) teaches while,

> Spontaneous platelet aggregation was a useful marker for survival and secondary coronary events among a cohort of patients *followed up for 5 years*...diverse measurements of platelet function...*are technically difficult to perform*. Physicians must distinguish between spontaneous platelet aggregation, which is induced by circulating agonists in the blood, and the response of platelets to agonists added externally.

See page 372.

Furthermore, the prior art demonstrates not only the high quantity of experimentation needed to carry out a method for "preventing" platelet aggregating conditions (e.g., arterial complications associated with atherosclerosis), but also teaches the unpredictability of carrying out such a method.

Hiatt, W. R. teaches (J Intern Med (2002) 251(3): 193-206, previously cited) the use of antiplatelet therapy for preventing atherothrombotic events in peripheral arterial disease. Specifically, Hiatt teaches studies determining the utility of antiplatelet therapy in preventing "arterial thrombotic complications associated with atherosclerosis" involve using many test subjects over a significant period of time. See Table 3, pg. 199. Even after such extensive trials, for example, "clinical trials have failed to demonstrate the anti-thrombotic efficacy of dipyridamole as monotherapy [80]. Dipyridamole and aspirin as combination therapy has been evaluated in several clinical trials with inconsistent results." See page 201, 2nd column). Finally, Hiatt teaches:

> "Studies evaluating the *early initiation of antiplatelet therapy in high-risk patients, duration of therapy* and the clinical utility of antiplatelet agents in *patients with advanced PAD undergoing endovascular procedure* will help define the role of these agents in the management of patients with PAD."

See page 203, 1st column.

Drouet, L. (Cerebrovasc Dis (2002) 13 Suppl 1: 1-6, previously cited) teaches :

"Antiplatelet therapy should also be considered in high-risk patients without a history of atherothrombotic events or current symptoms and in those with subclinical manifestation of atherothrombosis; however, *data from clinical trials in such patients are not yet available*...Thus, *clinical trials that are designed to evaluate the ability of antiplatelet agents to prevent such downstream damage are warranted in the future.*"

See page 5, 2nd column.

Therefore, the state of the art teaches the high quantity of experimentation needed for a method of "preventing" platelet aggregation, and the unpredictability of carrying out antiplatelet aggregation tests. The specification's teachings do not remedy this high quantity of experimentation or unpredictable level of experimentation.

(3) ***Quantity of Experimentation Necessary & the Unpredictability of the Art***

Case law has established that "(t)o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *In re Wright* 990 F.2d 1557, 1561. In *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) it was determined that "(t)he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art." The amount of guidance needed to enable the invention is related to the amount of knowledge in the art as well as the predictability in the art.

In the instant case, neither the art, nor the specification provides the necessary guidance or experimentation to enable one skilled in the art to "prevent" platelet aggregation in a patient (e.g., human). As demonstrated above, the specification provides limited guidance as to the treatment of atherosclerosis. Specifically, the specification only teaches treatment of humans

having atherosclerosis in which a *Chlamydia pneumoniae* infection "appeared" to play a role in the development of the atherosclerosis. The specification does not provide any examples of treating any individual (e.g., any mammal) with atherosclerosis (e.g., comprising individuals that do not have a *Chlamydia pneumoniae* infection) with the ketolides of the invention. Furthermore, while the specification teaches P- P_3 shows "good activity" in an in vitro platelet aggregation test, these results do not provide the skilled artisan the requisite guidance for "preventing" platelet aggregation in a patient (e.g., human) comprising "administering to a patient" (i.e., an in vivo administration) in need thereof an effective amount of a ketolide or its non-toxic, pharmaceutically acceptable salts sufficient to inhibit platelet aggregation in said patient.

In order to perform the experimentation required by the invention, the skilled artisan would have to obtain a cohort of individuals (e.g., any mammal) having a platelet aggregating condition and a control group of individuals not having a platelet aggregating condition, treating the individuals with the ketolides of the invention and measure the effect of the ketolide treatment over a period of many years to determine whether the administration of the ketolides "prevented" the platelet aggregation. Given the lack of guidance in the specification and the art, the results of this experimentation would be unpredictable, as the results would be based on a trial and error process with little to no starting point given by the specification. In essence, the experimentation that one skilled in the art would be required to perform is in fact the proposed novelty of the invention. However, "(I)t is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of the invention in order to constitute adequate enablement." (*Genetech Inc. v Novo Nordisk* 42 USPQ2d 1001).

Accordingly, in view of the unpredictability in the art and in view of the lack of specific disclosure in the specification, undue experimentation would be required to practice the invention as it is claimed.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claims 11-12 are rejected under 35 U.S.C. 102(e) as being anticipated by Leadlay et al. (USPN 6,437,151).

Due to the ambiguity of the claims (see 112, 2nd paragraph rejection above), the claims have been interpreted as being drawn to a method of preventing or inhibiting platelet aggregation in a patient comprising administering to said patient an effective amount of a ketolide or its non-toxic, pharmaceutically acceptable salts sufficient to inhibit platelet aggregation in said patient.

Leadlay teaches a method of treating a human with atherosclerosis (e.g., a platelet aggregating condition), in which *Chlamydia pneumoniae* appeared to play a role in the development of the atherosclerosis, using ketolides (see col. 4-11 and Examples 16-18, especially col. 11, lines 11-14). Accordingly, because Leadlay teaches ketolides are active against a platelet aggregating condition in which *Chlamydia pneumoniae* appeared to play a role (i.e., ketolides possess anti-infectious properties against *Chlamydia pneumoniae*), it is an

inherent property of the ketolides of Leadlay that the ketolides prevent or inhibit platelet aggregation.

Regarding Claim 12, Leadlay teaches the daily dosage is between 0.1-100 mg/kg (col. 12, lines 13-15).

10. Claims 11-12 are rejected under 35 U.S.C. 102(e) as being anticipated by Masamune et al. (USPN 6,025,350).

Due to the ambiguity of the claims (see 112, 2nd paragraph rejection above), the claims have been interpreted as being drawn to a method of preventing or inhibiting platelet aggregation in a patient comprising administering to said patient an effective amount of a ketolide or its non-toxic, pharmaceutically acceptable salts sufficient to inhibit platelet aggregation in said patient.

Masamune teaches a method of treating a human with atherosclerosis, in which *Chlamydia pneumoniae* appeared to play a role in the development of the atherosclerosis, using ketolides (see col. 1-15 and 65-72, especially col. 8, lines 41-43). Accordingly, because Masamune teaches ketolides are active against a platelet aggregating condition in which *Chlamydia pneumoniae* appeared to play a role (i.e., ketolides possess anti-infectious properties against *Chlamydia pneumoniae*), it is an inherent property of the ketolides of Masamune that the ketolides prevent or inhibit platelet aggregation.

Regarding Claim 10, Masamune teaches the daily dosage is between 0.2-200 mg/kg (col. 35, lines 20-27).

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 11-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shor et al. (USPN 5,424,187), in view of Agouridas et al. (USPN 5,747,467).

Due to the ambiguity of the claims (see 112, 2nd paragraph rejection above), the claims have been interpreted as being drawn to a method of preventing or inhibiting platelet aggregation in a patient comprising administering to said patient an effective amount of a ketolide or its non-toxic, pharmaceutically acceptable salts sufficient to inhibit platelet aggregation in said patient.

Shor teaches methods for treating arterial chlamydial granulomatous disease using anti-*Chlamydia pneumoniae* agents, such as erythromycins (see abstract; col. 2, line 67 to col. 3, line 10; col. 6, lines 49-56; col. 12, lines 40-54, for example). Shor further teaches that atherosclerotic lesions (i.e., atherosclerosis, a platelet aggregating condition) result from chlamydial granulomatous disease (see col. 7, lines 22-44 and Examples 2-8). Accordingly, Shor teaches treating a human with atherosclerosis, in which *Chlamydia pneumoniae* appeared to play a role in the development of the atherosclerosis, using erythromycins.

While Shor teaches the treatment using anti-*Chlamydia pneumoniae* agents, such as erythromycins, Shor does not teach using a ketolide, which is an erythromycin derivative.

However, Agouridas teaches ketolides are anti-*Chlamydia pneumoniae* agents (see col. 5). Specifically, Agouridas teaches a method of combatting Chlamydia infections in warm-blooded animals including humans comprising, administering to warm-blooded animals an effective amount of a ketolide or its non-toxic, pharmaceutically acceptable acid addition salts (col. 5, ln. 33-38).

Regarding Claim 12, the reference teaches that the usual daily dose is 1.5 to 6 mg/kg, and therefore, provides a range equivalent to the range provided in claim 10 (col. 5, lines 40-42). For example, if the daily dose was at 4mg/kg, and an individual to whom the ketolide was administered weighed 100 kg, then 400 mg would be administered to said individual per day.

Regarding Claims 13-17, Agouridas teaches the claimed ketolides (see cols. 1-5 and Example 3).

Accordingly, in view of the teachings of Agouridas, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Shor so as to have used the ketolides of Agouridas. One of ordinary skill in the art would have been motivated to modify the method of Shor, by using a ketolide of Agouridas, in order to have achieved the benefit of providing an effective method of treating a human with atherosclerosis, in which *Chlamydia pneumoniae* appeared to play a role in the development of the atherosclerosis, and therefore to have prevented or inhibited platelet aggregation. The ketolides of Agouridas would have provided Shor with the anti-*Chlamydia pneumoniae* agent necessary for inhibiting the granulomatous process, and therefore, providing an effective therapeutic

treatment (of preventing or inhibiting platelet aggregation) for a patient suffering from atherosclerosis (a platelet aggregating condition).

14. Claims 11-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shor et al. (USPN 5,424,187, previously cited), in view of Agouridas et al. (USPN 5,635,485).

Due to the ambiguity of the claims (see 112, 2nd paragraph rejection above), the claims have been interpreted as being drawn to a method of preventing or inhibiting platelet aggregation in a patient comprising administering to said patient an effective amount of a ketolide or its non-toxic, pharmaceutically acceptable salts sufficient to inhibit platelet aggregation in said patient.

Shor teaches methods for treating arterial chlamydial granulomatous disease using anti-*Chlamydia pneumoniae* agents, such as erythromycins (see abstract; col. 2, line 67 to col. 3, line 10; col. 6, lines 49-56; col. 12, lines 40-54, for example). Shor further teaches that atherosclerotic lesions (i.e., atherosclerosis, a platelet aggregating condition) result from chlamydial granulomatous disease (see col. 7, lines 22-44 and Examples 2-8). Accordingly, Shor teaches treating a human with atherosclerosis, in which *Chlamydia pneumoniae* appeared to play a role in the development of the atherosclerosis, using erythromycins.

While Shor teaches the treatment using anti-*Chlamydia pneumoniae* agents, such as erythromycins, Shor does not teach using a ketolide, which is an erythromycin derivative.

However, Agouridas teaches ketolides are anti-*Chlamydia pneumoniae* agents (see col. 6). Specifically, Agouridas teaches a method of combatting Chlamydia infections in warm-blooded animals including humans comprising, administering to warm-blooded animals an effective amount of a ketolide or its non-toxic, pharmaceutically acceptable acid addition salts (col. 6, ln. 55-59).

Regarding Claim 12, the reference teaches that the usual daily dose is 1.5 to 6 mg/kg, and therefore, provides a range equivalent to the range provided in claim 10 (col. 5, lines 40-42). For example, if the daily dose was at 4mg/kg, and an individual to whom the ketolide was administered weighed 100 kg, then 400 mg would be administered to said individual per day.

Regarding Claims 13-17, Agouridas teaches the claimed ketolides (see cols. 1-5 and Example 3).

Accordingly, in view of the teachings of Agouridas, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Shor so as to have used the ketolides of Agouridas. One of ordinary skill in the art would have been motivated to modify the method of Shor, by using a ketolide of Agouridas, in order to have achieved the benefit of providing an effective method of treating a human with atherosclerosis, in which *Chlamydia pneumoniae* appeared to play a role in the development of the atherosclerosis, and therefore to have prevented or inhibited platelet aggregation. The ketolides of Agouridas would have provided Shor with the anti-*Chlamydia pneumoniae* agent necessary for inhibiting the granulomatous process, and therefore, providing an effective therapeutic treatment (of preventing or inhibiting platelet aggregation) for a patient suffering from atherosclerosis (a platelet aggregating condition).

Conclusion

15. No claims are allowable.

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander H. Spiegler whose telephone number is (571) 272-0788. The examiner can normally be reached on Monday through Friday, 7:00 AM to 3:30 PM.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (571) 272-0782.

Papers related to this application may be faxed to Group 1637 via the PTO Fax Center using the fax number (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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